REMARKS

Applicants have amended the claims to more clearly describe the claimed invention. Support for the amendments may be found throughout the specification and in particular in claims 31, 32, and 47 of the application as filed; as well as at p. 13, l. 19 to p. 14, l. 3; at p. 12, l. 14 and l. 26; and in the Examples and Figures.

Restriction Requirement

Applicants thank the Examiner for entering the restriction requirement. Applicants acknowledge that the Examiner treated Applicants election of group I as an election without traverse. Applicants acknowledge that claims 39-56 are withdrawn from consideration at this time. Applicants acknowledge that the Examiner made the election of species referred to in the Office Action of 4/22/03 final.

Applicants acknowledge that the Examiner withdrew claims 22, 38, 18 and 19 from further consideration pursuant to 37 C.F.R. 1.142(b). Applicants note that there was no response filed on October 30, 2003 and request correction of this typographical error for the record. The undersigned discussed this rejection briefly with Examiner Schwadron on October 3, 2006 to obtain clarification before filing this reply.

Filing Dates of Provisional Applications

With the attached amendment to the specification, Applicants comply with the Examiner's requirement to amend the first paragraph of the specification to include the filing dates of the provisional applications.

Abstract

The Examiner objected to the Abstract as being too long. Applicants submit herein a new abstract and respectfully submit that the objection no longer applies to the newly submitted abstract.

Rejections under 35 U.S.C. § 102(b)

Weidanz et al.

The Examiner rejected claims 1, 2, 4-17, 23-27, 29-31, and 33-36 under 35 U.S.C. 102(b) as being anticipated by Weidanz et al. (WO 99118129). The Examiner analyzed Weidanz et al. as disclosing a TCR V_β /C_β attached by a linker to a V_α/C_α wherein said construct is linked to a human Ig κ constant region. The Examiner further stated that Weidanz et al. disclose use of various lengths of C_α and C_β regions wherein the C region is less than the native C region molecule and that such constant regions comprise the first nine amino acids of the TCR constant region. The Examiner further pointed out that Weidanz et al. disclose an in vivo method of treatment using this construct to treat a disease mediated by pathogenic T cells.

The Examiner further stated that the TCR chains used in the chimeric protein are derived from pathogenic T cells in the patient, citing to page 11 and pages 22-26. The Examiner continued, stating that Weidanz et al. disclose that the chimeric protein of the Weidanz et al. application can be made in insect cells using baculovirus. The Examiner then asserted that recitation of a particular means wherein the baculovirus produced chimeric protein is made carries no patentable weight. The Examiner finished his analysis by citing Weidanz et al. as teaching polyvalent multimers of the aforementioned chimeric TCR proteins wherein said molecules would have multiple constant region chains.

Applicants respectfully submit that this rejection no longer applies to the claims as amended. Although Weidanz et al. disclose a chimeric protein with V_α and V_β regions joined to a light chain constant region, Weidanz et al. do not disclose either or both a V_α or a V_β region joined to a IgG heavy chain constant region. The claims as amended are directed to a chimeric protein wherein one polypeptide of the chimeric protein comprises a V_α or V_β region, plus a portion of a constant region, plus a portion of an IgG heavy chain constant region; and the other polypeptide of the chimeric protein comprises the

other of the V_β or V_α region, plus a portion of a constant region, plus a portion of a light chain constant region. Additionally, although Weidanz et al. disclose fragments of the C_β regions, the fragment size as cited by the Examiner at Weidanz is larger in size than the C_β portion used in the instant invention.

McKeever et al.

The Examiner rejected claims 1, 2, 4-8, 10-13, 15-17, 23-27, 31, and 33-36 under 35 U.S.C. 102(b) as being anticipated by McKeever et al. The Examiner analyzed McKeever et al. as disclosing the administration of a chimeric TCR/IgGl construct to alter a T cell mediated pathology in a patient (wherein the treated mice are patients as defined in the specification, citing to the Summary and pages 1764-66). The Examiner cited to Figure 1 for a description of the construct used to produce the chimeric protein and notes that according to the Materials and Methods section, the protein was produced using a baculovirus expression system.

The Examiner then asserted that the recitation of a particular means used to produce the chimeric protein carries no patentable weight. The Examiner concluded his analysis by stating that the TCRs used in McKeever et al.'s chimeric protein "are derived from T cells which cause a pathology in the patient (p. 4)."

Applicants respectfully submit that this rejection no longer applies to the claims as amended. Although McKeever et al. disclose a chimeric protein with V_α and V_β regions joined to a heavy chain constant region, McKeever et al. do not disclose a V_α or a V_β region joined to a IgG light chain constant region. The claims as amended are directed to a chimeric protein wherein one polypeptide of the chimeric protein comprises a V_α or V_β region, plus a portion of a constant region, plus a portion of an IgG heavy chain constant region; and the other polypeptide of the chimeric protein comprises the other of the V_β or V_α region, plus a portion of a constant region, plus a portion of human κ or λ constant region.

Rejections under 35 U.S.C. § 103

Weidanz & Brostoff

The Examiner rejected claims 1, 2, 4-17, 23-27, 29-31, 33-37 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 99/18129) in view of Brostoff et at. (WO 94/25063).

The Examiner summarized Weidanz et al. as disclosing (1) a TCR V_β /C_β attached by a linker to a V_α/C_α wherein said construct is linked to human Ig κ constant regions; (2) the use of various lengths of C_α or C_β wherein the C region is less than the native C region molecule and that these Weidanz et al. C regions comprise the first nine amino acids of the TCR C region; (3) an in vivo method of treatment with said construct to treat disease mediated by pathogenic T cells where the TCR chains used in the chimeric protein are allegedly derived from pathogenic T cells in the patient; and (4) that the chimeric protein can be made in insect cells using baculovirus. The Examiner then asserted that the recitation of a particular means used to produce the chimeric protein carries no patentable weight. The Examiner finished his analysis by citing Weidanz et al. as teaching polyvalent multimers of the aforementioned chimeric TCR proteins wherein said molecules would have multiple constant region chains.

The Examiner then noted that although Weidanz et al. do not teach that their method can be used to treat T cell lymphoma, Brostoff et al. teach treatment of a T cell lymphoma by administration of TCR derived from a T cell lymphoma. The Examiner then asserted that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention.

Applicants respectfully submit that the rejection no longer applies to the claim as amended as Weidanz et al. no longer anticipate, nor do Weidanz et al. suggest, the chimeric proteins of the claimed invention. Further, the Examiner provided no motivation to combine the particular construct of Weidanz et al. with Brostoff et al. One

of ordinary skill in the art, motivated to treat T cell lymphoma, would have no motivation to select the particular constructs of Weidanz et al. to combine with Brostoff et al.

Weidanz & Lebowitz

The Examiner rejected claims 1-17, 23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 9911 81 29) in view of Lebowitz et al.

The Examiner summarized Weidanz et al. as disclosing (1) a TCR V_β/C_β attached by a linker to a V_α/C_α wherein said construct is linked to human Ig κ constant regions; (2) the use of various lengths of C_α or C_β wherein the C region is less than the native C region molecule and that these Weidanz et al. C regions comprise the first nine amino acids of the TCR C region; (3) an in vivo method of treatment with said construct to treat disease mediated by pathogenic T cells where the TCR chains used in the chimeric protein are allegedly derived from pathogenic T cells in the patient; and (4) that the chimeric protein can be made in insect cells using baculovirus. The Examiner then asserted that the recitation of a particular means used to produce the chimeric protein carries no patentable weight. The Examiner finished his analysis by citing Weidanz et al. as teaching polyvalent multimers of the aforementioned chimeric TCR proteins wherein said molecules would have multiple constant region chains.

The Examiner then noted that although Weidanz et al. do not teach that their method can be used to treat T cell lymphoma, Lebowitz et al. teach a "soluble high affinity chimeric TCR protein of claim 32." (P. 6) The Examiner asserted that one of skill in the art would be motivated to combine the references "because Lebowitz et al. teach that their chimeric TCR protein is soluble and of high affinity and can be used in vivo to treat disease." (P. 6)

Applicants respectfully submit that the rejection no longer applies to the claim as amended as neither Weidanz et al. no longer anticipate, nor do Weidanz et al. or nor Lebowitz et al. suggest, the chimeric proteins of the claimed invention. Further, the Examiner provided no motivation to combine the particular constructs of Weidanz et al.

with Lebowitz et al. One of ordinary skill in the art, motivated to treat T cell lymphoma, would have no motivation to select the constructs of Weidanz et al. to combine with the treatment disclosed by Lebowitz et al.

Weidanz et al. & Bonnem et al.

The Examiner rejected claims 1, 2, 4-17, 20, 21, 23-27, 29-31, 33-36 under 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 99/18129) in view of Bonnem et al. (WO 94/01133).

The Examiner summarized Weidanz et al. as disclosing (1) a TCR V_β/C_β attached by a linker to a V_α/C_α wherein said construct is linked to human Ig κ constant regions; (2) the use of various lengths of C_α or C_β wherein the C region is less than the native C region molecule and that these Weidanz et al. C regions comprise the first nine amino acids of the TCR C region; (3) an in vivo method of treatment with said construct to treat disease mediated by pathogenic T cells where the TCR chains used in the chimeric protein are allegedly derived from pathogenic T cells in the patient; and (4) that the chimeric protein can be made in insect cells using baculovirus. The Examiner then asserted that the recitation of a particular means used to produce the chimeric protein carries no patentable weight. The Examiner finished his analysis by citing Weidanz et al. as teaching polyvalent multimers of the aforementioned chimeric TCR proteins wherein said molecules would have multiple constant region chains.

The Examiner stated that although Weidanz does not teach that their methods can be used with GM-CSF, Bonnem discloses that GM-CSF can be administered to increase the immune response to an administered antigen.

Applicants respectfully submit that the rejection no longer applies to the claim as amended as Weidanz et al. no longer anticipate, nor do Weidanz et al. suggest, the chimeric proteins of the claimed invention.

Further, the Examiner provided no motivation to combine Weidanz et al. and Bonnem et al. One of ordinary skill in the art, motivated to treat T cell lymphoma, would

have no motivation to select the constructs of Weidanz et al. to combine with the GM-CSF administration of Bonnem et al. as Bonnem et al. teach the use of GM-CSF to increase the immune system's response to infectious diseases such as influenza (Example 2) and hepatitis B (Example 1).

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance.

This reply is filed on October 10, 2006. As the shortened statutory period for reply fell on Saturday, October 7, 2006, followed by the U.S. P.T.O. Columbus Day holiday on October 9, 2006, no fee is believed to be due in connection with this submission. However, if the Office determines that any fee is due, please charge Deposit Account No. 23-2415, referencing docket no. 30795-702.201.

If the Office believes, for any reason, that personal communication will expedite prosecution of this application, the Office is invited to telephone the undersigned at (858) 350-2309.

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Russell T. Boggs, Ph.D., Reg. No. 55,011

Date: October 10, 2006

650 Page Mill Road
Palo Alto, CA 94304
(650) 493-9300
Customer No. 021971